

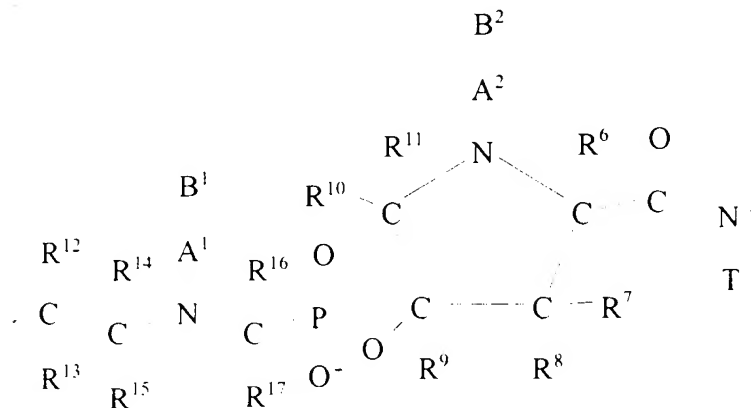
What is claimed is:

- 5 1. A method for detecting one or more nucleic acid molecules, comprising:

providing a sample that comprises at least one nucleic acid molecule;

10 contacting said sample with a solid support that comprises one or more attached oligonucleotide analogues under conditions that allow hybridization of one or more attached oligonucleotide analogues with nucleic acid molecules that are at least partially complementary to said one or more attached oligonucleotide analogue molecules.

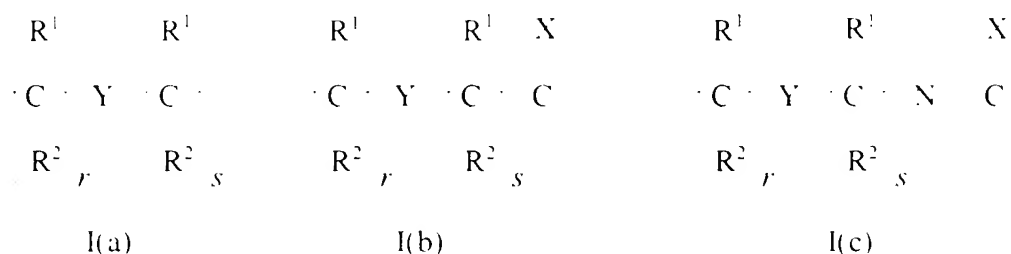
15 wherein at least one of said one or more attached oligonucleotide analogue molecules comprises the structure:



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wherein each B¹ and each B² is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic):



wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R^3 , R^4 , and R^5 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or an amino acid side chain;

Y is a single bond, O, S, or NR^4 ; and

X is O, S, Se, NR^5 , CH_2 , or $C(CH_3)_2$;

wherein each R^6 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein R^1 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or hydrogen, and R^2 is hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, aryl, aralkyl, or heteroaryl;

or R^1 is hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, aryl, aralkyl, or heteroaryl, and R^2 is hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or halogen;

wherein each R^3 is independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, alkoxy, aryl, arylalkyl, or heteroaryl;

wherein each R^{10} and each R^{11} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein each R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and each R^{17} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein T is hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein each R^{18} , R^{19} , R^{20} , and R^{21} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

n is 1 or greater, and;

detecting at least one nucleic acid molecule that is bound to said solid support.

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2. The method of claim 1, wherein said solid support is a membrane, chip, bead, or polymer.

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3. The method of claim 1, wherein the ratio of HypNA to pPNA monomers in at least one of said one or more attached oligonucleotide analogues is from 2:1 to 1:3.

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4. The method of claim 3, wherein the ration of HypNA to pPNA monomers in at least one of said one or more attached oligonucleotide analogues is from 1:1 to 1:2.

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5. The method of claim 1, wherein the lengths of said one or more attached oligonucleotide analogues is from 6 to 1,000 residues.

6. The method of claim 5, wherein the lengths of said one or more attached oligonucleotide analogues is from 12 to 60 residues.

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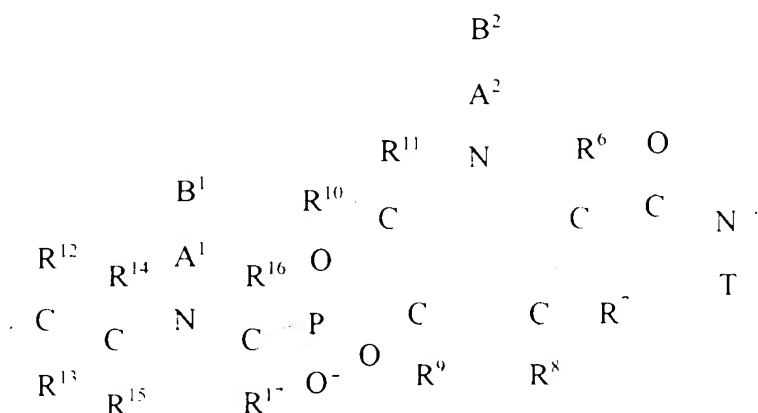
7. The method of claim 1, wherein said sample is a blood sample that is at least partially processed.

8. The method of claim 1, wherein said sample is a solution of at least partially purified DNA.

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9. The method of claim 1, wherein said detecting comprises staining with an intercalating nucleic acid stain.

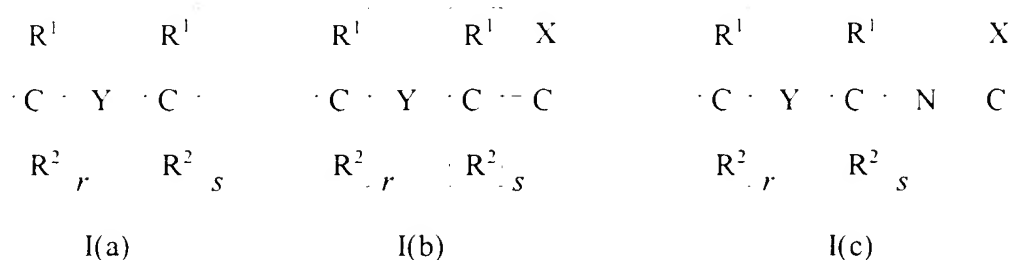
10. The method of claim 9, wherein said intercalating nucleic acid stain is selected from the group consisting of ethidium halides, ethidium dimers, monomeric cyanine dyes, or dimeric cyanine dyes.
- 5 11. The method of claim 1, wherein said detecting comprises detecting a label coupled to one or more nucleic acid molecules.
12. The method of claim 1, wherein said method is used to detect one or more SNPs.
- 10 13. The method of claim 1, wherein said method is used for expression profiling.
14. The method of claim 1, wherein said method is used to detect or identify a pathogen or contaminant.
- 15 15. A kit for the detection of one or more nucleic acid sequences, comprising:
- at least one oligonucleotide analogue molecule attached to a solid support, wherein said at least one oligonucleotide analogue molecule comprises the structure:
- 20



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wherein each B^1 and each B^2 is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic);



wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R^3 , R^4 , and R^5 , is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or an amino acid side chain;

Y is a single bond, O, S, or NR^4 ; and

X is O, S, Se, NR⁷, CH₂, or C(CH₃)₂;

5 wherein each R⁶ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

10 wherein R⁷ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or hydrogen, and R⁸ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, or heteroaryl;

15 or R⁷ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, or heteroaryl, and R⁸ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or halogen;

20 wherein each R⁹ is independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, alkoxy, aryl, arylkyl, or heteroaryl;

wherein each R¹⁰ and each R¹¹ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

25 wherein each R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, and each R¹⁷ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein T is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

5 wherein each R¹⁸, R¹⁹, R²⁰, and R²¹ is, independently, hydrogen, (C₁–C₆)alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

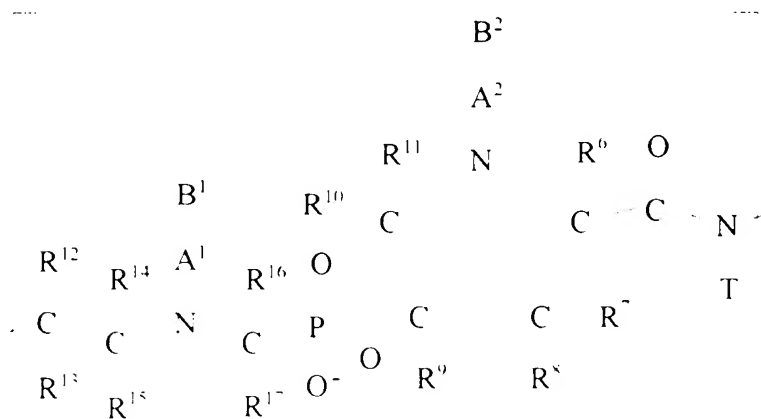
10 n is 1 or greater; and

at least one buffer, solution, or reagent useful in the detection of nucleic acid sequences.

15 16. A method for detecting one or more nucleic acid molecules, comprising:

providing a sample that comprises at least one nucleic acid molecule;

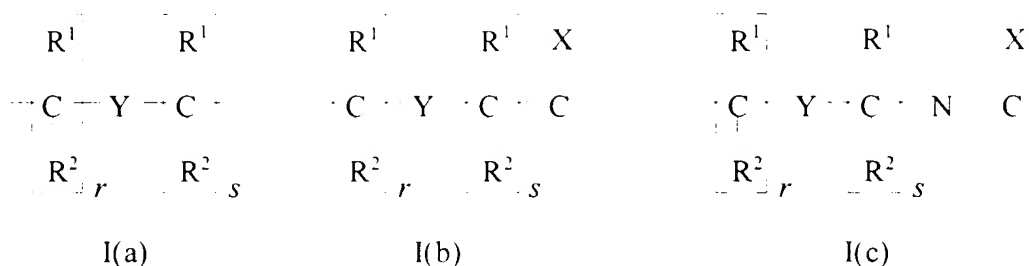
20 contacting said sample with one or more oligonucleotide analogue molecules under conditions that favor hybridization between nucleic acid molecules and oligonucleotide analogue molecules that are at least partially complementary, wherein said one or more oligonucleotide analogue molecules comprise the structure:



n

wherein each B^1 and each B^2 is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic);



wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R^3 , R^4 , and R^5 is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or an amino acid side chain;

Y is a single bond, O, S, or NR^4 ; and

X is O, S, Se, NR⁵, CH₂, or C(CH₃)₂;

5 wherein each R⁶ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

10 wherein R⁷ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or hydrogen, and R⁸ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, or heteroaryl;

15 or R⁷ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, or heteroaryl, and R⁸ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or halogen;

20 wherein each R⁹ is independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, alkoxy, aryl, aralkyl, or heteroaryl;

25 wherein each R¹⁰ and each R¹¹ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

30 wherein each R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, and each R¹⁷ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein T is hydrogen, (C₁ - C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁ - C₆)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

5 wherein each R¹⁸, R¹⁹, R²⁰, and R²¹ is, independently, hydrogen, (C1-C6)alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

10 *n* is 1 or greater;

capturing said oligonucleotide analogues to a solid support; and

detecting one or more nucleic acid molecules bound to said solid support.

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17. The method of claim 16, wherein said capturing is through a specific binding member attached to said one or more oligonucleotide analogues.

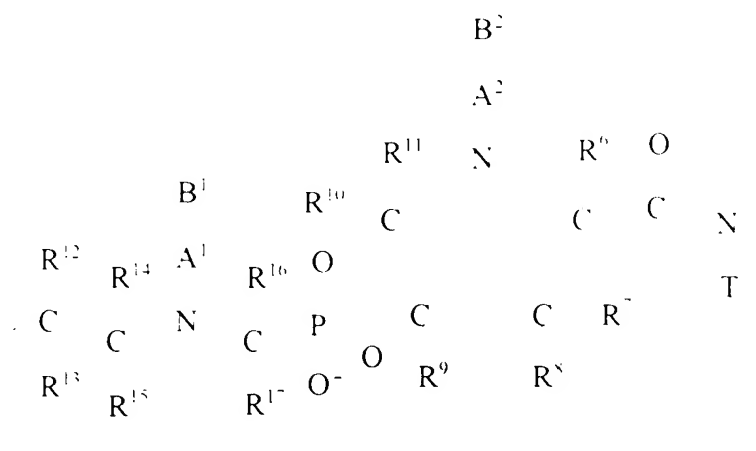
18. A method for separating, isolating, or purifying at least one nucleic acid molecule
20 from a population of nucleic acid molecules, comprising:

providing a population of nucleic acid molecules;

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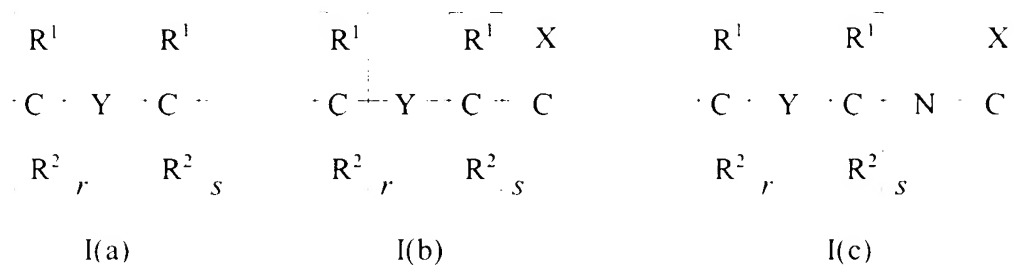
contacting the population of nucleic acid molecules with one or more capture probes comprising at least one oligonucleotide analogue under conditions that allow hybridization of nucleic acid molecules with oligonucleotide analogues, wherein said at least one oligonucleotide analogue comprises the structure:

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wherein each B^1 and each B^2 is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic);



wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen,

(C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted

(C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R³, R⁴, and R⁵, is, independently, hydrogen,

5 (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted

(C₁–C₆)alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or
an amino acid side chain;

Y is a single bond, O, S, or NR⁴; and

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X is O, S, Se, NR⁵, CH₂, or C(CH₃)₂;

wherein each R⁶ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-,

alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl,

15 heteroaryl, or an amino acid side chain;

wherein R⁷ is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-,

amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio,

amino, aryl, aralkyl, heteroaryl, or hydrogen, and R⁸ is hydrogen, (C₁–C₆)

20 alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl,
aryl, aralkyl, or heteroaryl;

or R⁷ is hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-

substituted (C₁–C₆)alkyl, aryl, aralkyl, or heteroaryl, and R⁸ is hydrogen,

(C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted

25 (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl,
or halogen;

wherein each R⁹ is independently, hydrogen, (C₁–C₆)alkyl, hydroxy-,

alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, alkoxy, aryl,

arylalkyl, or heteroaryl;

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wherein each R^{11} and each R^{12} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

5 wherein each R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and each R^{17} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

10 wherein T is hydrogen, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(C_1 - C_6)$ alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

15 wherein each R^{18} , R^{19} , R^{20} , and R^{21} is, independently, hydrogen, $(C_1 - C_6)$ alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

n is 1 or greater;

20 binding said capture probes to a solid support; and

separating at least one nucleic acid molecule that is hybridized to the one or more capture probes from the members of the population of nucleic acid molecules that are not bound to the capture probe.

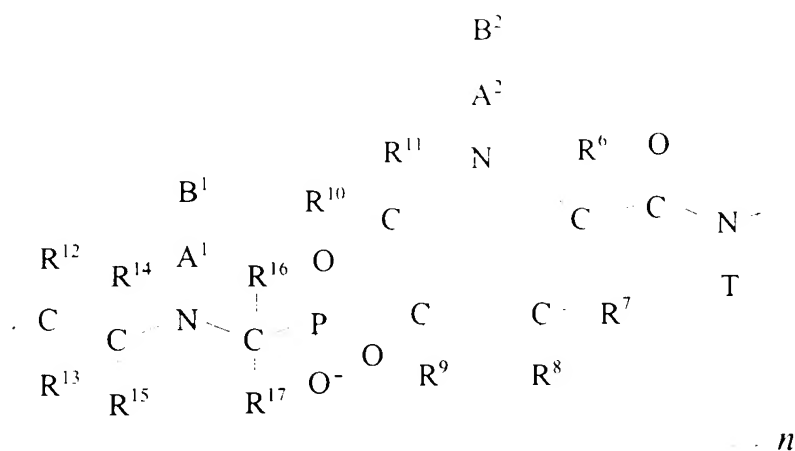
19. The method of claim 18, wherein said population of nucleic acid molecules
30 comprises RNA molecules.

20. The method of claim 18, wherein said one or more capture probes further comprises a specific binding member.
21. The method of claim 20, wherein said specific binding member is biotin.
- 5 22. The method of claim 18, wherein the ratio of HypNA to pPNA monomers in at least one of said one or more attached oligonucleotide analogues is from 2:1 to 1:3.
- 10 23. The method of claim 22, wherein the ration of HypNA to pPNA monomers in at least one of said one or more attached oligonucleotide analogues is from 1:1 to 1:2.
- 15 24. The method of claim 23, wherein said oligonucleotide analogue is a poly T oligomer.
25. A kit for the purification of poly A RNA, comprising:
- 20 a HypNA-pPNA poly T oligonucleotide analogue coupled to a first specific binding member;
beads coupled to a second specific binding member that can bind said first specific binding member; and
at least one buffer, solution, or reagent useful in the purification of RNA.
- 25 26. A kit for the purification of poly A RNA, comprising:
at least one biotin-conjugated oligonucleotide analogue;
streptavidin coated beads;
at least one buffer or solution; and
DEPC-treated water.
- 30

27. A method for inhibiting gene expression, comprising:

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administering an oligonucleotide analogue to at least one cell or at least one organism, wherein said oligonucleotide analogue comprises the structure:



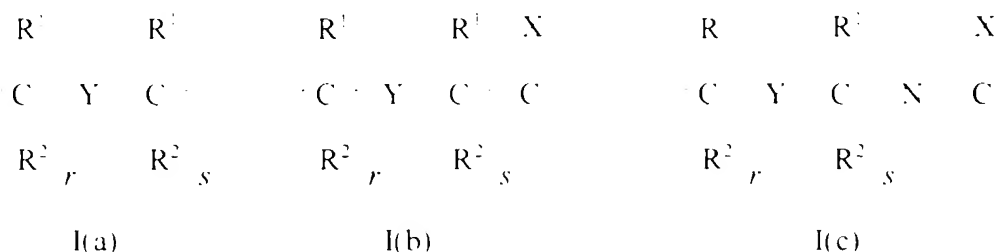
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wherein each B^1 and each B^2 is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

15

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic);

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wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R^3 , R^4 , and R^5 is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or an amino acid side chain;

Y is a single bond, O, S, or NR^4 ; and

X is O, S, Se, NR^5 , CH_2 , or $C(CH_3)_2$;

wherein each R^6 is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein R^7 is, independently, hydrogen, (C₁–C₆)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted (C₁–C₆)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or hydrogen, and R^8 is hydrogen, (C₁–C₆)

alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, or heteroaryl;

or R^7 is hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, or heteroaryl, and R^8 is hydrogen,

5 ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or halogen;

wherein each R^9 is independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, alkoxy, aryl,

10 aralkyl, or heteroaryl;

wherein each R^{10} and each R^{11} is, independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

15 wherein each R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and each R^{17} is, independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

20 wherein T is hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

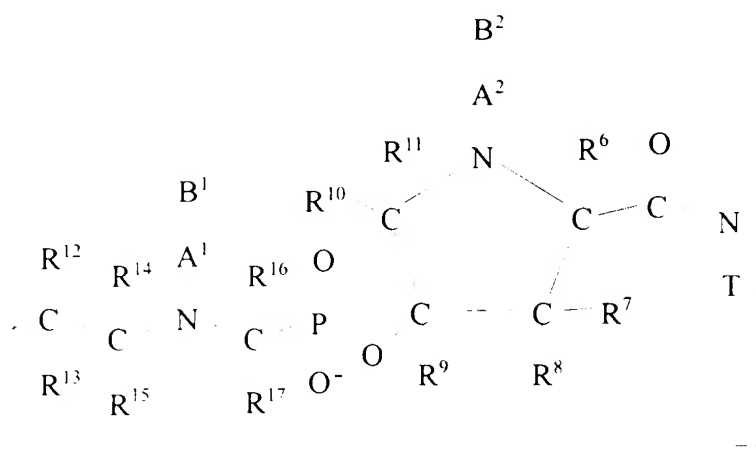
25 wherein each R^{18} , R^{19} , R^{20} , and R^{21} is, independently, hydrogen, ($C_1 - C_6$)alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

30 n is 1 or greater; and

inhibiting the expression of at least one gene that comprises sequences that are at least partially complementary to said oligonucleotide analogue.

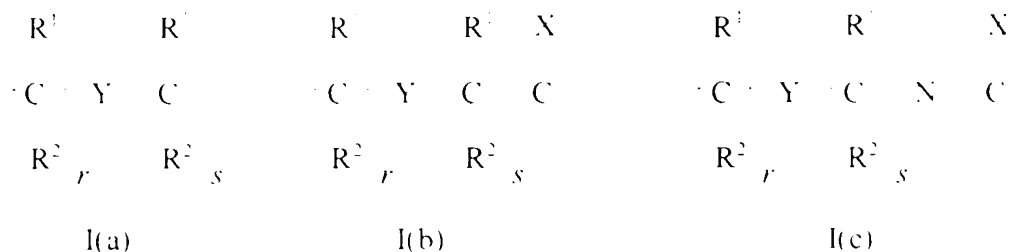
28. The method of claim 28, wherein the ratio of HypNA to pPNA monomers in said one oligonucleotide analogue is from 1:1 to 1:2.

29. A pharmaceutical composition for inhibiting gene expression, comprising at least one oligonucleotide analogue in a pharmacological formulation, wherein said oligonucleotide analogue comprises the structure:



wherein each B^1 and each B^2 is, independently, H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, or a reporter group, wherein amino groups are, optionally, protected by amino protecting groups;

wherein each A^1 and each A^2 is, independently, is a group of formula (Ia), (Ib), or (Ic);



wherein r and s are, for I(a) and I(b), independently of one another, values from 0 to 5 and are, for I(c), independently of one another, values from 1 to 5;

wherein each R^1 and each R^2 is, independently, hydrogen, $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, or halogen;

wherein each R^3 , R^4 , and R^5 is, independently, hydrogen, $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy, alkoxy, amino, aryl, aralkyl, heteroaryl, or an amino acid side chain;

Y is a single bond, O, S, or NR^4 ; and

X is O, S, Se, NR^5 , CH_2 , or $\text{C}(\text{CH}_3)_2$;

wherein each R^6 is, independently, hydrogen, $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(\text{C}_1 - \text{C}_6)$ alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

wherein R^7 is, independently, hydrogen, $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted $(\text{C}_1 - \text{C}_6)$ alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or hydrogen, and R^8 is hydrogen, $(\text{C}_1 - \text{C}_6)$

alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, or heteroaryl;

or R^7 is hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, or heteroaryl, and R^8 is hydrogen,

5 ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, amino, aryl, aralkyl, heteroaryl, or halogen;

wherein each R^9 is independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, alkoxy, aryl,

10 arylalkyl, or heteroaryl;

wherein each R^{10} and each R^{11} is, independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, aryl, aralkyl, heteroaryl, or an amino acid side chain;

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wherein each R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and each R^{17} is, independently, hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

20

wherein T is hydrogen, ($C_1 - C_6$)alkyl, hydroxy-, alkoxy-, amino-, or alkythio-substituted ($C_1 - C_6$)alkyl, hydroxy, alkoxy, alkylthio, aryl, aralkyl, heteroaryl, or an amino acid side chain;

25

wherein each R^{18} , R^{19} , R^{20} , and R^{21} is, independently, hydrogen, ($C_1 - C_6$)alkyl, an amino protecting group, a reporter group, an intercalator, a chelator, a linker, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide or oligonucleotide, or a soluble or nonsoluble polymer; and

30

n is 1 or greater.